DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Los Angeles District 9582461

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Certified Mail
Return Receipt Requested

WARNING LETTER

April 25, 2006 WL 19-06

Philip G. Shugart
President
Carolina Liquid Chemistries Corporation
510 West Central Avenue, Suite C
Brea, CA 92821

Dear Mr. Shugart:

During an inspection of your establishment located in Brea, California, on October 26 through November 8, 2005, our Investigator(s) determined that your firm manufactures and repackages in-vitro diagnostic devices. These in-vitro diagnostic devices are devices as defined by section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. 321(h), because they are intended for use in the cure, treatment, prevention, or diagnosis of a disease or medical condition, or affect the structure or any function of the body.

The above-stated inspection revealed that these devices are adulterated under section 501(h) of the Act, 21 U.S.C. 351(h), in that the methods used in, or the facilities or controls used for, their manufacture, packing, storage, or installation are not in conformance with the Current Good Manufacturing Practice (CGMP) requirements for medical devices which are set forth in the Quality System regulation, as specified in Title 21, Code of Federal Regulations (CFR), Part 820. Significant deviations include, but are not limited to, the following:

1. Failure to establish a quality plan defining the quality practices, resources, and activities relevant to devices that are designed and manufactured, as required by 21 CFR 820.20(d).

2. Failure to follow procedures for conducting management reviews at defined intervals and frequency, as required by 21 CFR 820.20(c). Specifically, no documented management reviews have been performed from 2003 through the current inspection.

requirements and other applicable provisions of the Act. Additionally, there was no documentation of training for auditors designated to conduct internal audits.

11. Failure to ensure that labels and labeling used for each lot of finished devices are properly documented and kept in the device history record (DHR), as required by 21 CFR 820.120(d). Specifically, 11 of 11 device history records reviewed did not contain any reference to the direction inserts enclosed with the finished device kits.

Additionally, your HCY 60 Homocysteine Reagent Kit, Homocysteine Reagent Kit CC201-AO, CK200 Creatine Kinase Reagent Kit, and AST 200 Aspartate Transaminase Reagent Kit are adulterated under section 501(f)(1)(B), 21 U.S.C. 351(f)(1)(B) of the Act, for failure to obtain FDA premarket approval, and misbranded under section 502(o), 21 U.S.C. 352(o) of the Act, for failure to notify the agency of your intent to introduce the devices into commercial distribution, as required by section 510(k), 21 U.S.C. 360(k) of the Act. For a product requiring premarket approval before marketing, the notification required by section 510(k), 21 U.S.C. 360(k) is deemed to be satisfied when a premarket approval application (PMA) is pending before the agency, 21 CFR 907.81(b).

A premarket notification is required under section 510(k), 21 U.S.C. 360(k) of the Act, and 21 CFR 807 (a)(3)(i), for the modifications to the following devices: (1) HCY 60 Homocysteine Reagent Kits are taken from bulk reagent containers and poured into special "cartridges" or bottles used by CLC and then affixed with CLC's own label. Additionally, the labeling specification for the reagents are changed to use the reagents on a specific analyzer, Beckman Synchron, as opposed to testing human patient samples by the manual method or general automated chemistry analyzer. (2) Homocysteine Reagent Kits CC201-AO are taken from bulk reagent containers and poured into smaller bottles and prepared as a "kit" for analysis including a package insert with directions for use for manual determinations and with general chemistry analyzer parameters. This is a change from the bulk manual method to a smaller kit sized method with general parameter instructions. (3)The CK200 Creatine Kinase Reagent Kit's manufacturing process is changed from the bulk supplier in that there is no reagent preparation required verses mixing by the bulk supplier including differences in sensitivity and stability and there is a change in use of the reagent on the Beckman Synchron as opposed to general automated chemistry analyzer. (4) AST 200 Aspartate Transaminase Reagent Kit design is changed from the bulk supplier in that the labeling is changed to use the reagent on the Beckman Synchron as opposed to testing human patient samples by the manual method or general automated chemistry analyzer. These devices are not exempt from premarket notification under 21 CFR 807.85 because you have made changes that affect the device. Specifically, you have changed the intended use of the bulk reagent by changing the labeling, as well as the other changes noted above.

Furthermore, your HCY 60 Homocysteine Reagent Kit, Homocysteine Reagent Kit CC201-AO, and Cocaine Metabolic Reagent COCM COCAINE are misbranded under 502(o), 21 U.S.C. 352(o), in that the devices were not included in a list required by

section 510(j), 21 U.S.C. 360(j).

Our inspection also disclosed that your does not have written procedures for medical device reporting, as required by section 519, 21 U.S.C. 360i of the Act and 21 CFR Part 803 (Medical Device Reporting regulation). Therefore, your devices are further misbranded within the meaning of Section 502(t)(2), 21 U.S.C. 352(t)(2) in that your firm failed to furnish information required by or under section 519 and 21 CFR Part 803.

In addition, your firm failed to report a product corrective action to FDA or maintain a written justification for not reporting the correction or removal action to FDA, as required by 21 CFR 806.20. Therefore, your device is further misbranded under Section 502(t)(2), 21 U.S.C 352(t)(2) of the Act for failing to comply with Section 519(f), 21 U.S.C.360i(f) of the Act.

We also acknowledge receipt of your written response dated November 22, 2005 with attachments. The response is not adequate because, although it addresses many of the revisions that have been made to your quality system procedures, it does not specify that these activities have been completed or will be completed in a timely manner. Several of your proposed timeframes for completion are quite long and not acceptable. Your response also does not address our concerns regarding the pre-marketing clearances, device listing, and correction and removal deficiencies disclosed during our inspection.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA 483 issued at the close of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. You also must promptly initiate permanent corrective and preventive action on your quality system.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, no premarket approval applications for Class III devices to which the Quality System regulation deficiencies are reasonably related will be approved until the violations have been corrected. Also, no requests for Certificates to Foreign Governments will be granted until the violations related to the subject devices have been corrected.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil money penalties.

Please notify this office in writing within fifteen (15) working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action

3. Failure to follow procedures for conducting quality audits, as required by 21 CFR 820.22. Specifically, no documented quality audits to verify that the quality system is effective in fulfilling the firm's quality system objectives have been performed from 2003 up through the current inspection.

4. Failure to follow procedures for addressing the documentation of nonconforming product as required by 21 CFR 820.90(b)(1). Specifically, 400 bottles of Glucose Reagent that were initially quarantined were subsequently released into distribution without documentation of evaluation and justification.

5. Failure to ensure that a process, whose results cannot be fully verified by subsequent inspection and test, has been validated and approved according to established procedures, as required by 21 CFR 820.75(a). Specifically, there is no documentation of process validation activities and results for cleaning, de-ionized water and cap torque processes.

6. Failure to establish and maintain complaint handling procedures to ensure that all complaints are processed in a uniform and timely manner as required by 21 CFR 820.198(a)(1). Specifically, complaint procedures do not define timeliness for processing complaints or require justification for deciding not to investigate complaints involving possible failure of a device to meet any of its specifications, including but not limited to leaking cartridges.

7. Failure to establish procedures to control the design process of a device to ensure that specified design requirements are met, as required by 21 CFR 820.30(a).

8. Failure to establish procedures to ensure that all purchased or otherwise received products and services conform to specified requirements as required by 21 CFR 820.50. Specifically, you do not have procedures regarding the type and extent of control to be exercised over suppliers, contractors, and consultants.

9. Failure to establish procedures to ensure that equipment is routinely calibrated, checked and maintained for adherence to applicable equipment maintenance schedules, as required by 21 CFR 820.70(g)(2). Specifically, there is no documentation for the calibration, checking, and maintenance activities for the peristaltic pump, mechanical pipette, [redacted] analyzer, thermometers used to evaluate temperatures of refrigerators and freezers, and other pieces equipment used in the production and testing of your devices.

10. Failure to establish procedures for identifying training needs and ensuring that employee training is documented, as required by 21 CFR 820.25. Specifically, there is no documentation demonstrating training of production and quality system employees in the requirements set forth in their quality policy and quality system requirements to ensure compliance with the Quality System Regulation

cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

If you have any questions relating to this letter please contact Senior Compliance Officer, Dannie E. Rowland at 949-608-4448. You may obtain general information about all of FDA's requirements for manufacturers of medical devices through the Internet at http://www.fda.gov.

Please submit your response to:

Pamela B. Schweikert
Director, Compliance Branch
Food and Drug Administration
19701 Fairchild
Irvine, CA 92612-2445

Sincerely,

Alonza E. Cruse
District Director
Los Angeles District Office

Cc: Department of Health Services
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